Original Research

# Evaluation of the management of acute cholecystitis in very elderly patients



Aim: The objective of this study was to evaluate the characteristics and management of AC in very elderly (>80 years old) patients.

Material and Methods: A total of 345 patients aged 20-89 years, who presented to the emergency department of our hospital and were diagnosed with acute cholecystitis were included in the study. The patients were divided into two groups as < 80 years old and ≥80 years old, and the studied parameters were compared between these two groups. Patients' demographic data such as age and gender, comorbidities, duration of hospitalization, treatment method, type of cholecystectomy and mortality status were recorded.

Results: The majority of the patients in the ≥ 80 yo group had comorbidities, including hypertension by 39.3%, coronary artery disease by 19.2%, diabetes mellitus by 18.5% and cerebrovascular disease by 14.5%. The rate of the patients undergoing urgent surgery was significantly higher in the ≥ 80 yo group (p=0.02). The rate of the patients undergoing elective surgery was significantly higher in the < 80 yo group (p<0.01). The duration of hospitalization was significantly longer in the patients ≥ 80 yo. No mortality was observed in the <80 yo group, while eight (4.6%) patients in the ≥ 80 yo group died.

Discussion: The management of acute and chronic diseases in very old patients has become important due to the globally increasing elderly population and the corresponding increase in life expectancy. According to our findings, comorbidities, biochemical parameters, hospitalization and mortality were significantly higher in the patients ≥80 yo compared to those <80 yo.

Acute Cholecystitis, Cholecystectomy, Comorbidity, Surgical Treatment, Very Elderly

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### Introduction

Acute cholecystitis (AC), namely gallbladder inflammation, is a severe condition associated with symptoms of upper abdominal pain, fever, and leukocytosis, and sometimes accompanied by gallstones with a mortality rate of about 3% [1, 2]. However, this rate increases with age. Eventually, 20-40% of asymptomatic patients with gallstones develop AC [3]. AC is an important indication for hospitalizations and is associated with an increased economic burden on the health care system [4]. AC leads to complications that require urgent surgery such as gallbladder perforation, gangrene, emphysematous cholecystitis and empyema. Risk factors for these complications include advanced age, male gender, and associated diseases such as diabetes mellitus (DM), fever and significant leukocytosis [5]. In the elderly, AC is one of the most serious conditions requiring surgical treatment. The elderly are especially at high risk for AC, and 6% of elderly patients develop severe AC [6]. The prevalence of gallstones, which is the most common cause of AC, is 15% and 24% in men and women aged 70 years, while these rates increase to 24% and 25% in men and women aged 90 years, respectively [7].

Early laparoscopic cholecystectomy is the treatment of choice for AC in young patients [8, 9]. Whereas in elderly AC patients, characteristics of the disease, comorbidities, and poor functional status make surgical management of AC challenging in this population. The management of AC is contradictory due to the reduced physiological reserve in these patients, and it can cause serious morbidity and mortality [10]. According to the 2017 United Nations report, it is estimated that the population over the age of 60 will increase from 25% to 35% in Europe and from 12.5% to 25% in Asia by 2050 (available at: https://esa. un.org/unpd/wpp/ Publications/Files/WPP2017\_KeyFindings. pdf). Global increase in life expectancy makes the management of AC in very elderly patients an important issue to investigate [11].

Although there are studies on the management of AC in elderly patients, the literature data on this subject in very elderly patients are limited. Therefore, the objective of this study was to evaluate the characteristics and management of AC in very elderly (>80 years old) patients.

### Material and Methods

### Study Design

A total of 345 patients aged 20-89 years, who were admitted to the emergency department of our hospital, and were diagnosed with acute cholecystitis and treated between 2010 and 2020 were retrospectively analyzed. The patients were divided into two groups as < 80 years old and ≥80 years old, and the studied parameters were compared between these two groups.

Patients referred from the emergency department to our clinic with the presumed diagnosis of AC were included in the study. Patients with recurrent AC, concurrent acute cholangitis, pancreatitis, gastrointestinal cancer, or biliary tract diseases were excluded from the study.

## Data Collection

Patients' demographic data such as age and gender, comorbidities, biochemical parameters including WBC, NEU (%), NEU, urea and creatinine, duration of hospitalization,

treatment method, percutaneous drainage status, type of cholecystectomy and mortality status were obtained from the information system of our hospital and recorded.

### Management of the Patients

Blood tests and abdominal sonography were performed to the patients who presented to the emergency department of our hospital with signs and symptoms compatible with AC. When necessary, abdominal CT or MR cholangiography was performed. The diagnosis of AC was based on clinical and laboratory findings, and ultrasonography criteria. In the clinical evaluation, Murphy's sign, acute upper abdominal pain, right hypochondrial tenderness and fever >37.5oC were investigated. Among the laboratory parameters, the white blood cell (WBC) count of 10x109/L was diagnostic. Ultrasonographic findings included a >5 mm thickened and edematous bladder, distended bladder, pericholecystic fluid and gallstones [12].

Follow-up of the patients was terminated after cholecystectomy in patients who underwent surgery (urgent or elective). Complications and mortality within 30 days were taken into account in all patients. Cholecystectomy operations were categorized as urgent (within 48 hours of hospitalization) or elective (after 48 hours).

All patients were first evaluated in the emergency department and analgesia, proton pump inhibitor, antimicrobial therapy, IV fluid therapy were initiated. The patients were then referred to the wards to receive medical or surgical treatment according to the clinical judgment and the patient's request. Although laparoscopic cholecystectomy was the standard treatment method, some patients continued antibiotherapy without surgery due to several reasons such as advanced age, comorbidity, concurrent anticoagulant therapy, >7 days symptom duration or patient's refusal to have surgery. All surgeries were performed by the same team.

## **Ethical Considerations**

Before the beginning of the study, necessary ethical approval was received from the local ethics committee of our hospital. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

### Statistical Analysis

Data obtained in the study were statistically analyzed using SPSS v. 23 (SPSS, Statistical Package for Social Sciences) for Windows statistical software. The normality of the data was evaluated with the Kolmogorov-Smirnov test. Continuous variables were expressed as means, and categorical variables as frequency and percentage. Mann-Whitney U and Chi-square tests were used in the comparison of the quantitative and qualitative variables between the groups, respectively. The p-values <0.05 were considered statistically significant.

### Results

A total of 345 patients aged 20-80 years were included in the study. Patients were divided into two groups as < 80 yo (n:172) and  $\geq$  80 yo (n:173). Data of the patients were obtained from the information system of the hospital and compared between the two groups. The mean age was 48.49 years in the <80 yo group and 85.73 years in the  $\geq$  80 yo group. In the <80 yo group, 61.6% (n:106) of the patients were female and 38.4% (n:66) were male, while in the  $\geq$  80 yo group, 60.7% (n:105)

of the patients were female and 39.3% (n:68) were male. No significant difference was found between the groups in terms of gender.

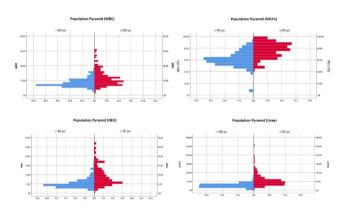
When comorbidities of the patients were examined, the most common comorbidity was hypertension (HT) in both groups. The majority of the patients in the ≥ 80 yo group had comorbidities, including HT by 39.3%, coronary artery disease (CAD) by 19.2%, DM by 18.5% and cerebrovascular disease (CVD) by 14.5%. In biochemical tests, WBC, NELL (%), NELL urea, and creatining

In biochemical tests, WBC, NEU (%), NEU, urea and creatinine values were statistically significantly higher in the  $\geq$  80 yo group compared to <80 yo group (for all p<0.05) (Table 1). The distribution of WBC, NEU(%), NEU and urea values according to the groups is shown in Figure 1.

When treatment methods were examined, urgent surgeries

**Table 1.** Comparison of biochemical parameters between the groups

Parameter	Age group	n	Mean Rank	U	р
	0.0				
Wbc	< 80 yo	172	139,62	9137	<0.01
	≥ 80 yo	173	206,18		
NEU (%)	< 80 yo	172	120,07	5774	<0.01
	≥ 80 yo	173	225,62		
NEU (%)	< 80 yo	172	127,89	7119	<0.01
	≥ 80 yo	173	217,85		
Urea	< 80 yo	172	112,38	4451	<0.01
	≥ 80 yo	173	233,27		
Creatinine	< 80 yo	172	122,38	6170,5	<0.01
	≥ 80 yo	173	223,33		



**Figure 1.** Distribution of WBC, NEU(%), NEU and urea values according to the groups

Population Pyramid (Hospitalization)

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**Figure 2.** Distribution of the duration of hospitalization according to the groups

were performed in 8.7% (n:15) of the patients <80 yo and 20.8% (n:36) of the patients  $\geq$  80 yo. The difference between the two groups was statistically significant, and the rate of the patients undergoing urgent surgery was significantly higher in the  $\geq$  80 yo group (p=0.02). Elective surgery was performed in 91.3% (n:157) of the patients <80 yo and 13.3% (n:23) of the patients  $\geq$  80 yo. Accordingly, the rate of the patients undergoing elective surgery was significantly higher in the patients <80 yo (p<0.01). When the type of the cholecystectomy was examined, while laparoscopic surgery was performed in 93.62% (n:161) and open surgery in 6.4% (n:11) of the patients <80 yo, 20.2% (n:35) of the patients  $\geq$  80 yo underwent laparoscopic surgery and 13.9% (n:11). n:24) open surgery.

Medical therapy alone was not applied in the <80 yo group, while 65.9% (n:114) of the patients in the  $\geq$  80 yo group underwent medical therapy (p<0.01). 91.3% (n:157) of patients <80 yo and 13.3% (n:23) of patients  $\geq$  80 yo had medical treatment + surgery. Accordingly, the rate of the patients who underwent medical therapy plus surgery was statistically significantly higher in the patients < 80 yo (p<0.01). While percutaneous drainage was not applied in any patient in the <80 yo group, 15% (n:26) of the patients  $\geq$  80 yo underwent percutaneous drainage.

It was determined that in the patients <80 yo, the duration of hospitalization differed significantly according to the type of cholecystectomy performed. The duration of hospitalization was significantly longer in the patients who underwent open surgery compared to laparoscopic cholecystectomy (p<0.01). In addition, in the patients  $\geq$  80 yo, the duration of hospitalization was significantly longer in the patients who underwent open cholecystectomy compared to those administered medical therapy alone (p<0.01). The distribution of the duration of hospitalization according to the groups is presented in Figure 2. While only one (0.6%) patient in the <80 yo group was admitted to the intensive care unit (ICU), 41 (23.7%) patients in the  $\geq$  80 yo group were admitted to the ICU. No mortality was observed in the <80 yo group, while eight (4.6%) patients in the  $\geq$  80 yo group died.

### Discussion

AC is an increasing problem in the elderly with the global increase in the elderly population. Although with the advances in medicine, the general health status of elderly patients has improved, the presence of comorbidities in this age group complicates the management of AC. Currently, there is no consensus on the management of AC in very elderly patients, and studies on this subject are limited in the literature. In the present study, clinical features and management AC were retrospectively analyzed in 365 patients and compared between the patients < 80 yo and those  $\geq$  80 yo.

It is known that comorbidities limit treatment options in patients over 80 years of age. [6, 13]. In addition, these patients often have a previous history of biliary disease and concomitant choledocholithiasis [10], which makes treatment difficult together with general status of the patient. The prevalence of comorbidities in elderly patients also makes it difficult to compare the parameters of AC management between young and elderly patients [14].

In a study by Feldman et al. comparing medical and surgical treatment methods in elderly patients with AC, the most common comorbidities were chronic renal failure, congestive heart disease, DM, HT, and CVD [15]. Similarly, in a study by Amaral et al., the most common comorbidities in elderly patients with AC were reported as DM, cardiac diseases and HT, and the rate of comorbidities were significantly higher in the elderly patients compared to young patients [16].

The presence of comorbidities affects the decision for operation. In a study by Nielsen et al, 413 patients >65 yo were evaluated, and multiple comorbidities were found in the majority of the patients. However, the authors proposed that multiple morbidities should not preclude the decision for surgical intervention [17]. In the present study, the presence of comorbidities was significantly higher in the patients ≥80 yo compared to those <80 yo. The most common comorbidities in this group included CAD, HT, DM and CVD. Despite the differences between studies, the most common comorbidities seem to be hypertension, DM, and cardiac diseases in elderly patients with AC. We think that a multidisciplinary approach is needed to minimize the effects of comorbidities, especially in the surgical management of elderly patients.

Some of the laboratory parameters are diagnostic for AC, and a WBC count > 10x109/L was used as a diagnostic criterion in our study. Among the studied laboratory parameters, WBC, NEU(%), NEU, urea and creatinine values were statistically significantly higher in the  $\geq 80$  yo group compared to < 80 yo group (for all p<0.05). A study by Lulleci et al. compared laboratory findings of AC between the elderly and non-elderly patients, WBC count was significantly higher in the elderly group [18]. Similarly Parker et al. reported elevated WBC counts in 59% of the elderly patients [19]. In another study, WBC count was reported to be a risk factor for clinical outcomes [6]. These results may be due to aging immunopathology.

Cholecystectomy is the definitive treatment for AC, and early cholecystectomy is preferred in young patients and even in carefully selected elderly patients [11, 20, 21]. However, many centers prefer conservative treatment and delaying surgery for an elective procedure in elderly patients with AC. Elective laparoscopic cholecystectomy has been reported as an appropriate method for the management of elderly patients with AC [17]. Elective cholecystectomy should be planned for patients in whom urgent intervention is not possible and if there are no contraindications [3]. Nevertheless, urgent laparoscopic cholecystectomy is a commonly used method [22]. In our study, 20.8% of the patients  $\geq$  80 yo underwent urgent and 13.3% elective surgery. Of the patients in this group, 65.9% received conservative medical therapy.

Laparoscopic cholecystectomy is a useful approach for the treatment of acute cholecystitis in elderly patients with its advantages such as less pain, shorter hospitalization and minimal invasiveness [16]. However, the optimal treatment of AC is controversial in elderly patients and with the aging population, addressing this issue is becoming an increasingly urgent necessity. In our study, open cholecystectomy was performed only in cases where laparoscopy was not considered safe due to comorbidities or local conditions. Accordingly, open cholecystectomy was performed in 24 (13.9%) patients ≥ 80

yo. In a study by Serban et al., the rate of open cholecystectomy was reported to be higher in elderly patients [14].

It is known that postoperative complications are higher and the hospital stay is longer in elderly patients who have undergone surgery [23]. In our study, the duration of hospitalization was longer in patients who underwent open surgery compared to laparoscopy in both groups. In addition, duration of hospitalization was significantly longer in the patients  $\geq$  80 yo. In the study by Serban et al., length of stay in the hospital was longer in patients undergoing open surgery and those >80 yo [14].

The risk of mortality increases with age in elderly patients with AC. In a meta-analysis by Kamarajah et al. including 99 studies, mortality was found to increase by 10 folds in patients  $\geq$  80 yo [24]. In our study, while no mortality was observed in the < 80 yo group, the mortality rate was found as 4.6% (n:8) in patients  $\geq$  80 yo. Open cholecystectomy was performed in all 8 deceased patients. In a study by Escartin et al. on the management of AC in very elderly patients, the mortality rate was reported as 4% in the operated patients > 85.4 yo [3]. However, high mortality rates of 17.5% have been reported in high-risk elderly patients [25].

### Study Limitations

This study has some limitations. It was designed as a retrospective study and conducted in a single center. In addition, the follow-up data could not be analyzed. However, the relatively high number of patients is the strength of the study. Considering the scarcity of studies in the literature on the management of AC in very elderly patients, we think that our findings may guide future studies on this subject.

### Conclusion

The management of acute and chronic diseases in very old patients has become important due to the globally increasing elderly population and the corresponding increase in life expectancy. According to our findings, comorbidities, biochemical parameters, hospitalization and mortality were significantly higher in the patients ≥80 yo compared to those <80 yo. However, there is a need for further multicenter prospective randomized controlled studies on AC management in very elderly patients.

### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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### Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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